$$A_s = \frac{a+b}{2a}$$

where:

a = Horizontal distance from point of ascent to point of maximum peak height; and

b = Horizontal distance from the point of maximum peak height to point of descent.

The asymmetry factor (A_s) is satisfactory if it is not more than 1.3.

(*2*) *Efficiency of the column.* From the number of theoretical plates (n) calculated as described in §436.216(c)(2) of this chapter calculate the reduced plate height (h_r) as follows:

$$h_r = \frac{(L)(10{,}000)}{(n)(d_p)}$$

where:

L = Length of the column in centimeters;

n = Number of theoretical plates; and

d_p = Average diameter of the particles in the analytical column packing in micrometers.

The absolute efficiency (h_r) is satisfactory if it is not more than 15.

(*3*) *Resolution factor.* The resolution factor (R) between the peak for clindamycin phosphate and the peak for clindamycin hydrochloride in the chromatogram of the resolution test solution is satisfactory if it is not less than 6.0.

(*4*) *Coefficient of variation* (*relative standard deviation*). The coefficient of variation (S_R in percent) of 5 replicate injections of the working standard solution (prepared as directed in paragraph (b)(1)(ii)(*b*)(*1*) of this section is satisfactory if it is not more than 2.5 percent.

If the system suitability parameters have been met, then proceed as described in §436.216(b) of this chapter.

(*d*) *Calculations.* Calculate the clindamycin content as follows:

$$\text{Milligrams of clindamycin per milliliter} = \frac{A_u \times P_s \times d}{A_s \times 1{,}000}$$

where:

A_u = Area of the clindamycin phosphate peak in the chromatogram of the sample (at a retention time equal to that observed for the standard);

A_s = Area of the clindamycin phosphate peak in the chromatogram of the clindamycin phosphate working standard;

P_s = Clindamycin activity in the clindamycin phosphate working standard solution in micrograms per milliliter; and

d = Dilution factor of the sample.

(2) *Sterility.* Proceed as directed in §436.20 of this chapter, using the method described in paragraph (e)(1) of that section.

(3) *Pyrogens.* Proceed as directed in §436.32(a) of this chapter, using a solution containing the equivalent of 24 milligrams of clindamycin per milliliter.

(4) [Reserved]

(5) *Depressor substances.* Proceed as directed in §436.35 of this chapter.

(6) *pH.* Proceed as directed in §436.202 of this chapter, using the undiluted drug.

[39 FR 19161, May 30, 1974, as amended at 46 FR 60568, Dec. 11, 1981; 50 FR 19921, May 13, 1985; 54 FR 43289, Oct. 24, 1989; 55 FR 5842, Feb. 20, 1990]

§ 453.230 Lincomycin hydrochloride injection.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Lincomycin hydrochloride injection is an aqueous solution of lincomycin hydrochloride monohydrate containing benzyl alcohol as a preservative. Each immediate container contains either 1, 2, or 10 milliliters of a solution containing, in each milliliter, 300 milligrams of lincomycin, and 9 milligrams of benzyl alcohol. The lincomycin content is satisfactory if it is not less than 90 percent and not more than 120 percent of the number of milligrams of lincomycin that it is represented to contain. It is sterile. It is nonpyrogenic. It contains no depressor substances. Its pH is not less than 3.0 and not more than 5.5. The lincomycin hydrochloride monohydrate used conforms to the standards prescribed by

§ 453.30a(a)(1) (i), (vi), (vii), (viii), (ix), (x), and (xi).

(2) *Labeling.* It shall be labeled in accordance with the requirements of § 432.5 of this chapter. If each immediate container contains only 1 milliliter of the drug, the labeling shall include the statement ''For pediatric use''.

(3) *Requests for certification; samples.* In addition to complying with the requirements of § 431.1 of this chapter, each such request shall contain:

(i) Results of tests and assays on:

(*a*) The lincomycin hydrochloride monohydrate used in making the batch for potency, moisture, pH, specific rotation, infrared absorption spectrum, lincomycin B content, identity, and crystallinity.

(*b*) The batch for potency, sterility, pyrogens, depressor substances, and pH.

(ii) Samples required:

(*a*) The lincomycin hydrochloride monohydrate used in making the batch: 10 packages, each containing approximately 300 milligrams.

(*b*) The batch:

(*1*) For all tests except sterility: A minimum of 10 immediate containers.

(*2*) For sterility testing: 20 immediate containers, collected at regular intervals throughout each filling operation.

(b) *Tests and methods of assay*—(1) *Potency.* Use either of the following methods; however, the results obtained from the gas liquid chromatography assay shall be conclusive.

(i) *Microbiological turbidimetric assay.* Proceed as directed in § 436.106 of this chapter, preparing the sample for assay as follows: Using a suitable hypodermic needle and syringe, remove all of the withdrawable contents if it is represented as a single-dose container; or, if the labeling specifies the amount of potency in a given volume of the resultant preparation, remove an accurately measured representative portion from each container. Place the portion, thus obtained, into a suitably-sized volumetric flask and dilute to volume with sterile distilled water. Remove an aliquot and further dilute with sterile distilled water to the reference concentration of 0.5 microgram of lincomycin per milliliter (estimated).

(ii) *Gas liquid chromatography assay.* Proceed as directed in § 436.306 of this chapter, except prepare the sample for assay as follows: Dilute the equivalent of 300 milligrams of lincomycin to 50 milliliters with methanol and shake. Transfer a 3-milliliter aliquot to a 10-milliliter volumetric flask and make to mark with methanol. Place a 2-milliliter aliquot into a 15-milliliter centrifuge tube and evaporate to dryness on a steam bath with a stream of dry air. Dissolve the residue in 1 milliliter of dry pyridine. Calculate the lincomycin content as follows:

$$\text{Lincomycin content in milligrams per milliliter} = \frac{R_u \times W_s \times d \times f}{R_s \times \text{number of milliliters of sample}}$$

where:

$$R_u = \frac{\text{Area of lincomycin sample peak}}{\text{Area of internal standard}}$$

$$R_s = \frac{\text{Area of lincomycin standard peak}}{\text{Area of internal standard}}$$

W_s=Weight of lincomycin working standard in milligrams;

d=Dilution factor;

f=Potency of lincomycin working standard in milligrams of lincomycin per milligram

(2) *Sterility.* Proceed as directed in § 436.20 of this chapter, using the method described in paragraph (e)(1) of that section.

(3) [Reserved]

(4) *Pyrogens.* Proceed as directed in § 436.32(a) of this chapter, using a solution containing 0.5 milligram of lincomycin per milliliter.

(5) *Depressor substances.* Proceed as directed in § 436.35 of this chapter.

(6) *pH.* Proceed as directed in § 436.202 of this chapter, using the undiluted solution.

[39 FR 19161, May 30, 1974, as amended at 46 FR 3841, Jan. 16, 1981; 46 FR 60568, Dec. 11, 1981; 50 FR 19921, May 13, 1985]

Subparts D–E—[Reserved]

Subpart F—Dermatologic Dosage Forms

§ 453.522 Clindamycin phosphate dermatologic dosage forms.

§ 453.522a Clindamycin phosphate topical solution.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Clindamycin phosphate is a solution of clindamycin phosphate in a suitable and harmless vehicle. Each milliliter contains 10 milligrams of clindamycin activity. Its clindamycin content is satisfactory if it is not less than 90 percent and not more than 110 percent of the number of milligrams of clindamycin that it is represented to contain. Its pH is not less than 4.0 and not more than 7.0. The clindamycin phosphate used conforms to the standards prescribed by § 453.22(a)(1).

(2) *Labeling.* It shall be labeled in accordance with the requirements of § 432.5 of this chapter.

(3) *Requests for certification; samples.* In addition to complying with the requirements of § 431.1 of this chapter, each such request shall contain:

(i) Results of tests and assays on:

(*a*) The clindamycin phosphate used in making the batch for clindamycin content, microbiological activity, moisture, pH, crystallinity, and identity.

(*b*) The batch for clindamycin content and pH.

(ii) Samples required:

(*a*) The clindamycin phosphate used in making the batch: 6 packages, each containing approximately 300 milligrams.

(*b*) The batch: A minimum of six immediate containers.

(b) *Tests and methods of assay*—(1) *Clindamycin content* (*vapor phase chromatography*). Proceed as directed in § 436.304 of this chapter, except prepare the sample for assay and calculate the clindamycin content as follows:

(i) *Preparation of the sample.* Accurately transfer a volume of sample equivalent to approximately 20 milligrams of clindamycin activity to a 50-milliliter volumetric flask. Evaporate the sample to near dryness under a stream of nitrogen. Dilute to 50 milliliters with pH 9.0 borate buffer and mix well. Place 25.0 milliliters of this solution into a 50-milliliter stoppered centrifuge tube. Add 10 milliliters of chloroform. Shake vigorously for 15 minutes and centrifuge to obtain adequate phase separation of the chloroform and aqueous phase. Transfer 20 milliliters of the aqueous phase from the tube into a 35-milliliter stoppered centrifuge tube. Add to the tube a weighed amount of intestinal alkaline phosphatase equivalent to 50 units of activity[1] and allow to stand until the phosphatase has dissolved completely. Place the centrifuge tube into a water bath at 37° C ± 2° C for 2.5 hours. After the 2.5-hours hydrolysis, allow the solution to cool.

(ii) *Calculations.* Calculate the clindamycin content as follows:

$$\text{Clindamycin content per milliliter} = (R_u \times W \times_s \times d \times f)/(R_s \times V)$$

where:

R_u=Area of clindamycin sample peak/Area of internal standard;

R_s=Area of clindamycin standard peak/Area of internal standard;

W_s=Weight of clindamycin working standard in milligrams;

d=Dilution factor;

f=Potency of clindamycin working standard in milligrams of clindamycin per milligram;

V=Volume of sample in milliliters.

(2) *pH.* Proceed as directed in § 436.202 of this chapter, using the undiluted drug.

[46 FR 2997, Jan. 13, 1981. Redesignated at 54 FR 38224, Sept. 15, 1989]

§ 453.522b Clindamycin phosphate gel.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Clindamycin phosphate gel contains clindamycin phosphate in a suitable and harmless vehicle. Each gram contains clindamycin phosphate equivalent to 10 milligrams of clindamycin activity. Its clindamycin content is satisfactory if it is not less than 90 percent and not more than 110 percent of the number of milligrams of

[1] Defined such that 50 units hydrolyzes at least 20 micromoles of a clindamycin phosphate authentic sample under the assay conditions described in § 436.304 of this chapter.